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Etherification of alkoxydialkylsilanes with carbonyl compounds

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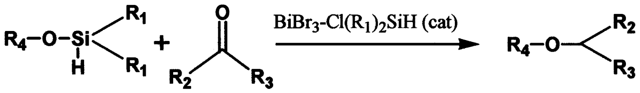
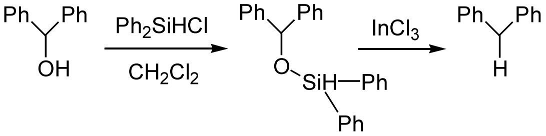
Abstract—A novel method for preparing ethers from alkoxydialkylsilanes and carbonyl compounds through reductive etherification is described. The salient feature in this method is the utilization of internal hydrogen as the hydride source for reducing the oxonium intermediate generated by using the $Cl(R)_2SiBr[BiBr_3/Cl(R)_2SiH]$ catalytic system. © 2002 Published by Elsevier Science Ltd.

In a previous communication[1] we reported an efficient reductive etherification of alcohols with carbonyl compounds through the intermediacy of different trialkylsilyl ethers using the $BiBr_3/Et_3SiH$ catalytic system. The active catalyst was deduced to be as triethylsilyl bromide by NMR studies and by verifying that commercial triethylsilyl bromide works as the catalyst for this purpose. In that method triethylsilane was used in excess as the reducing agent. To make the method more efficient in terms of atom economy, we investigated the possibility of using alkoxydialkylsilanes as intermediates in these reductive etherifications using a $BiBr_3$–$Cl(R)_2SiH$ catalytic system.



In these alkoxysilanes, the H present in the molecule is expected to serve as an internal reducing agent. A recent report by Baba[2] on the use of chlorodiphenylsilane with catalytic amount of indium trichloride for reductive deoxygenation of secondary and tertiary alcohols to alkanes gave further impetus to this study. In the present communication we report the results of our investigations, which led to a novel method for ether formation by hydride transfer.



Alkoxydialkylsilanes used in the present study are readily prepared[3,5] in high yields from the corresponding alcohols and chlorodiisopropylsilane using DMAP. The reductive etherification was first tried with benzyloxydiisopropylsilane and benzaldehyde in the presence of bismuth bromide, and the expected product was isolated in 57% yield after overnight at room temperature. Addition of 0.1 equiv. of chlorodiisopropylsilane accelerated this reaction and the reaction went to 96% conversion in 20 min. The best conditions[4] for this reductive etherification are the use of catalytic $BiBr_3$/chlorodiisopropylsilane in acetonitrile at room temperature followed by the addition of alkoxysilane and the carbonyl compound. The results[6] obtained using this method are summarized in Table 1.

Treatment of benzyloxydiisopropylsilane with aliphatic or aromatic aldehydes and ketone (entries 1, 2 and 3) afforded the corresponding ethers in 88–90% yield. Under these conditions, reacting a optically pure alkoxysilane with an aldehyde (entry 9) gave the corresponding ether in good yield with complete retention of stereochemistry. It is also noteworthy that alkoxysilane with a halide substituent can be used for this alkylation giving the alkylated product in 91% yield (entry 7). However, alkylation of silane derived from (*R*)-(−)-pantolactone (entry 10) was not successful.

As in the case of reductive etherification of trialkyl silyl ethers described in the previous communication using bismuth bromide–triethylsilane, we observed precipitation of the metal during the reaction. NMR studies confirmed the interaction of $BiBr_3$ with alkoxydialkylsi-

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Keywords: alkoxydialkylsilanes; $Cl(R)_2SiBr[BiBr_3/Cl(R)_2SiH]$; reductive etherification.

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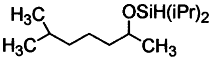
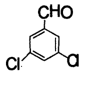
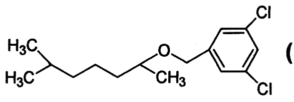
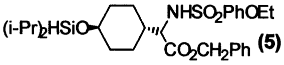
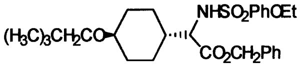
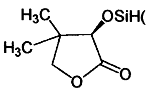
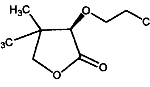
Table 1. Ether formation from alkoxysilanes and carbonyl compounds

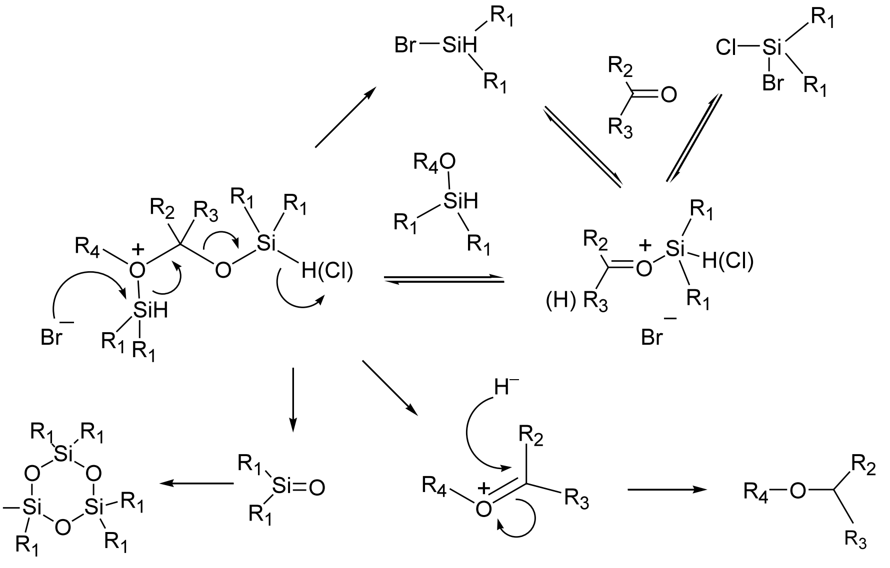
Entry	Alkoxysilane	Carbonyl compound	Product	Yield (%)
1	$PhCH_2OSiH(i\text{-}Pr)_2$ **(1)**	PhCHO	$(PhCH_2O)_2$ **(7)**	90
2		$(CH_3)_3CHO$	$PhCH_2OCH_2C(CH_3)_3$ **(8)**	89
3		CH_3COCH_3	$PhCH_2OCH(CH_3)_2$ **(9)**	88
4	$Ph(CH_2)_2OSiH(i\text{-}Pr)_2$ **(2)**	CH_3COCH_3	$Ph(CH_2)_2OCH(CH_3)_2$ **(10)**	91
5		CH_3CH_2CHO	$Ph(CH_2)_2OCH_2CH_2CH_3$ **(11)**	82
6		(*trans*)- PhCH=CHCHO	$Ph(CH_2)_2OCH_2CHCHPh$ (*trans*) **(12)**	89
7	$Br(CH_2)_3OSiH(i\text{-}Pr)_2$ **(3)**	PhCHO	$Br(CH_2)_3OCH_2Ph$ **(13)**	91
8	 **(4)**		 **(14)**	85
9	 **(5)**	$(CH_3)_3CCHO$	 **(15)**	92
10	 **(6)**	CH_3CH_2CHO	 **(16)**	trace

lane or chlorodiisopropylsilane in acetonitrile leading to the formation of the corresponding bromodiisopropylsilane, Bi metal, and HBr, which adds to acetonitrile.[7]

An interesting byproduct that was isolated was the trisiloxane shown in Scheme 1, which oiled out during the reaction. This byproduct was characterized by spectroscopy and authenticated by comparison with the literature.[8]

These results are in agreement with the conclusions drawn in the previous communication, and accordingly the active catalyst in this case is proposed to be the corresponding to the –SiH that was used. The mechanistic details are shown in Scheme 1.

In conclusion, an efficient method for reductive etherification of alkoxydialkylsilanes via internal hydride transfer using $Cl(R)_2SiBr$ ($BiBr_3$–$Cl(R)_2SiH$) as the catalyst is described.



Scheme 1. Reductive etherification of alkoxydialkylsilanes.

References

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2. Yasuda, M.; Onishi, Y.; Ueba, M.; Miyai, T.; Baba, A. *J. Org. Chem*. **2001**, *66*, 7741–7744.
3. **Typical procedure for the preparation of alkoxydiisopropylsilanes**: A 250 mL three-necked flask, equipped with a thermocouple, condenser and a magnetic stirrer was charged with an alcohol (30 mmol), 90 mL of THF, DMAP (6 mmol) and triethylamine (60 mmol). Chlorodiisopropylsilane (36 mmol) was slowly added to the solution. The resulting solution was stirred at 25°C overnight or heated to 50°C and maintained at this temperature for 2 h. After the reaction was completed (monitored by TLC or HPLC), the solid was filtered, and the filtrate was evaporated under reduced pressure. The residue was extracted with 150 mL of TBME, washed with 50 mL of water and 50 mL of saturated sodium chloride, and dried over magnesium sulfate. Evaporation of organic solvent afforded a colorless liquid, which was further purified by silica column chromatography.
4. **Typical procedure for etherification**: A flask was charged with bismuth bromide (0.35 mmol) and 10 mL of acetonitrile, followed by the addition of chlorodiisopropylsilane (0.45 mmol) and alkoxydiisopropylsilane (4.5 mmol) in 5.0 mL of acetonitrile. The fine black suspension was formed within a couple of minutes. Then, the aldehyde or ketone (5.4 mmol) was slowly added. The reaction was exothermic, and the formation of an oil was observed within 10 min. After the reaction was completed (monitored by TLC or HPLC), acetonitrile was evaporated. The residue was extracted with 100 mL of TBME and washed with 20 mL of water. The organic layer was dried over magnesium sulfate and evaporated under reduced pressure. The crude was purified on a silica column with an EtOAc/hexane eluent system to give the desired product.
5. NMR data on silanes: (**1**) ^{1}H δ 1.00–1.06 (m, 14H), 4.25 (s, 1H), 4.80 (s, 2H), 7.24–7.34 (m, 5H). ^{13}C δ 13.3, 17.5, 67.8, 126.7, 127.5, 128.6, 141.3. (**2**) ^{1}H δ 0.99–1.04 (m, 14H), 2.86 (t, J=7.35 Hz, 2H), 3.89 (t, J=7.35 Hz, 2H), 4.12 (s, 1H), 7.20–7.30 (m, 5H); ^{13}C δ 13.4, 24.4, 39.7, 67.2, 125.7, 127.8, 129.4, 145.9. (**3**) ^{1}H δ 0.90–0.98 (m, 14H), 1.92–2.04 (m, 2H), 3.46 (t, J=6.4 Hz, 2H), 3.77 (t, J=5.85 Hz, 2H), 4.08 (s, 1H). ^{13}C δ 12.3, 17.7, 26.3, 35.8, 63.3. (**4**) ^{1}H δ 0.79 (d, J=6.6 Hz, 6H), 0.87–1.08 (m, 14H), 1.15 (d, J=6.8 Hz, 3H), 1.20–1.51 (m, 7H), 3.62–3.80 (m, 1H), 4.11 (s, 1H). ^{13}C δ 12.4, 13.6, 17.2, 18.5, 22.3, 24.2, 27.5, 28.9, 71.4. (**5**) ^{1}H δ 0.91–0.95 (m, 14H), 0.92–1.25 (m, 4H), 1.37 (t, J=6.9 Hz, 3H), 1.41–1.62 (m, 3H), 1.79–1.98 (m, 2H), 3.28–3.41 (m, 1H), 3.61–3.70 (m, 1H), 3.98 (q, J=6.9 Hz, 2H), 4.05 (s, 1H), 4.72 (d, J=7.5 Hz, 1H), 4.80 (d, J=7.5 Hz, 1H), 4.97 (d, J=10 Hz, 1H), 6.79 (d, J=8.8 Hz, 2H), 7.09–7.19 (m, 2H), 7.26–7.28 (m, 3H), 7.62 (d, J=8.1 Hz, 2H). ^{13}C δ 12.8, 17.8, 26.2, 27.8, 35.0, 40.5, 60.2, 64.3, 67.7, 73.4, 114.9, 128.6, 129.0, 129.5, 129.8, 131.2, 135.1, 162.8, 171.6. (**6**) ^{1}H δ 1.01–1.13 (m, 14H), 1.19 (s, 3H), 1.24 (s, 3H), 3.89 (d, J=9.2 Hz, 1H), 3.99 (d, J=9.2 Hz, 1H), 4.12 (s, 1H), 4.33 (s, 1H); ^{13}C δ 12.8, 17.8, 19.5, 23.3, 41.6, 76.0, 78.9, 175.8.
6. NMR data on ethers: Compounds **7**–**13** and **15** are known and the NMR data are identical to those reported in the literature. NMR data for the two new compounds are as follows: **14** ^{1}H δ 0.80 (d, J=6.6 Hz, 6H), 1.02–1.10 (m, 2H), 1.12 (d, J=6.8 Hz, 3H), 1.20–1.51 (m, 5H), 3.40–3.42 (m, 1H), 4.32 (d, J=13 Hz, 1H), 4.43 (d, J=13 Hz, 1H), 7.15 (s, 1H), 7.16 (s, 1H), 7.18 (s, 1H); ^{13}C δ 20.0, 22.9, 23.6, 28.4, 37.2, 39.4, 69.2, 76.0, 126.1, 127.8, 135.2, 143.2; MS $C_{15}H_{22}OCl_2$, 273 (M−16).
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